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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/539,415

03/20/2006

Dharmaraj Ramachandra Rao

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EXAMINER

CHU, YONG LIANG

ART UNIT

PAPER NUMBER

1626

MAIL DATE

DELIVERY MODE

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/539,415	<b>Applicant(s)</b> RAO ET AL.	
	<b>Examiner</b> YONG CHU	<b>Art Unit</b> 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 28 December 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-6 and 18-22 is/are pending in the application.
- 4a) Of the above claim(s) 18-22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-6 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>03/20/2006, 03/21/2006; and 09/27/2007</u> .                  | 6) <input type="checkbox"/> Other: _____                          |



## **DETAILED ACTION**

Claims 1-6, and 18-22 are currently pending in the instant application.

### ***Information Disclosure Statement***

Applicant's Information Disclosure Statements, filed on 03/20/2006, 03/21/2006, and 09/27/2007 have been considered. Please refer to Applicant's copies of the PTO-1449 submitted herewith.

### ***Priority***

This Application is a 371 of PCT/GB03/05357, filed on 12/10/2003, claims the benefit of foreign priority of UK0229583.0, filed on 12/19/2002.

### ***Response to Restriction Requirements***

The response to the restriction request with election of Group I (i.e. claims 1-6, drawn to a process of preparing (+)-duloxetine or its acid salt) *without traverse* by Applicants' representative, Mr. Thomas P. Pavelko dated on 12/28/2007, has been considered.

### ***Status of the Claims***

Claims 18-22 are withdrawn from further consideration by the Examiner due to restriction requirement dated on 08/13/2007 as being drawn to non-elected inventions under 37 CFR 1.142(b). Therefore, claims 1-6 will be examined on the merits.

### ***Specification***

The instant specification is objected to for mis-spelling “?” at pages 10-12.

Appropriate correction is required.

### ***Claim Rejections - 35 USC § 102(b)***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 2 are rejected under 35 U.S.C. 102 (b) as being anticipated by Robertson et al., *U.S. Patent No. 4,956,388* (“the `388 patent”).

Applicants’ instant elected invention of claims 1 and 2 is drawn to a process for preparing (+)duloxetine, or an acid addition salt thereof comprising:

- 1) resolving racemic ( $\pm$ )duloxetine with a chiral acid ( e.g. dibenzoyl tartaric acid) to obtain a salt of the chiral acid and (+)duloxetine;
- 2) if desired, converting the salt prepared in step (1) to the free base or a further acid addition salt.

The `388 patent disclosed a process for preparing (+)duloxetine as Example 14 in Column 11 by “resolving the racemic mixture” at lines 46-55, column 5. The `388 patent further taught that this resolution can be carried out in the presence of a resolving agent by repeated crystallization. Particularly useful resolving agents include

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dibenzoyl -d- and -l-tartaric acids (a chiral acid) and the like. Such teachings anticipate the instant claims 1 and 2.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6 are rejected under 35 U.S.C. 103 (a) as unpatentable over the '388 patent in view of the teachings of *U.S. Patent No. 3,830,806* ("the '806 patent"), and Wheeler et al. *Journal of Labelled Compounds and Radiopharmaceuticals*, **1996**, Vol. 36, 3, pp.213-223, ("Wheeler et al.").

Applicants' instant elected invention of claims 1, and 2 is drawn to a process for preparing (+)duloxetine, or an acid addition salt thereof comprising:

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- 1) resolving racemic ( $\pm$ )duloxetine with a chiral acid ( e.g. dibenzoyl tartaric acid, di-p-dibenzoyl tartaric acid, etc.) to obtain a salt of the chiral acid and (+)duloxetine;
- 2) if desired, converting the salt prepared in step (1) to the free base or a further acid addition salt (e.g. hydrochloride salt).
- 3) if desired, repeating recrystallization steps.

Determination of the scope and content of the prior art (MPEP §2141.01)

The `388 patent disclosed a process for preparing (+)duloxetine as Example 14 in Column 11 by “resolving the racemic mixture” at lines 46-55, column 5. The `388 patent further taught that this resolution can be carried out in the presence of a resolving agent by repeated crystallization. Particularly useful resolving agents include dibenzoyl -d- and -l-tartaric acids and the like.

The `806 patent specifically taught that the chiral acids (referred as “optically active acids”) mandelic acid, tartaric acid, dibenzoyl-tartaric acid, di-p-toluyl-tartaric acid, and campharic acid could be used for racemic mixture resolution at lines 73, column 8 through lines 7, column 9.

Wheeler et al. taught duloxetine hydrochloride salt and its clinical application.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between the `388 patent process and the instantly claimed process is that the `388 patent did not specifically teach what “dibenzoyl -d- and -l-tartaric acid, or the like” is.

*Finding of prima facie obviousness - rationale and motivation (MPEP § 2142-2413)*

However, such difference would have been obvious for one having ordinary skill in the art at the time the invention, because the '806 patent" specifically taught that the chiral acids (referred as "optically active acids") mandelic acid, tartaric acid, dibenzoyl-tartaric acid, di-p-toluyl-tartaric acid, and campharic acid could be used for racemic mixture resolution at lines 73, column 8 through lines 7, column 9. The step (3) of the instantly claimed process is also taught and suggested in the '388 patent as by carrying out the recrystallization process repeatedly. In terms of the step of further converting the salts prepared in step (1) to hydrochloride salt is obvious to one ordinary skilled in the art, because such duloxetine hydrochloride salt has been taught by Wheeler et al.

Therefore, the instantly claimed invention is obviousness to one ordinary skilled in the art.

***Conclusion***

No claims are allowed.

***Telephone Inquiry***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong Chu whose telephone number is 571-272-5759. The examiner can normally be reached on 7:00 am - 3:30 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph M<sup>c</sup>Kane can be reached on 571-272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.



Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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